

REMARKS

Claims 4-6, 8, 9, 11, 12, 14, 19, 20, 23, and 33-41 are now pending in this application. Claims 4-6, 8, 9, 11, 12, 14, 19, 20, and 23 have been rejected. 1-3, 7, 10, 13, 15-18, 21, 22, and 24-32 are cancelled herein. New claims 33-41 are added. Claims 4-6, 8, 9, 11, 12, 14, 19, 20, and 23 are amended herein to clarify the invention.

The Examiner has requested that Applicants confirm the oral election of Group III (claims 1, 4-6, 8, 9, 11, 12, 14, 15, 17-20, 23, 24, 26, 27, 29, 30, and 32) as drawn to a hyperthermia agent and a method for using a cytokine and hyperthermia for treatment of a malignant tumor. Applicants hereby confirm such election.

Applicants' attorney and the Examiner had a telephone conversation regarding the subject matter of binding an antibody to the surface of the magnetic particles be included in Group III. The Examiner stated that for now, the claims directed to the binding of an antibody to the surface of the magnetic particles are directed to a non-elected invention but that if Applicants add such subject matter in new claims the Examiner will reconsider whether to add them to Group III. New claims 37 and 38 are directed to the antibodies, which are used to improve the selectivity of the magnetic particles to act on the cancer

cells. It is respectfully requested that claims 37 and 38 be examined with the other claims of the present application.

Claims 2, 3, 7, 10, 13, 16, 21, 22, 25, 28, and 31 have been withdrawn from further consideration as being drawn to non-elected inventions. These claims have been cancelled.

Claims 4, 6, 15, 17, 18, 24, 26-30, and 32 have been objected to for being drawn to a non-elected invention or being dependent from a claim directed to a non-elected Group. Appropriate action has been taken by either modifying claim dependencies or cancelling claims.

Claim 20 has been rejected under 35 U.S.C. § 112, second paragraph, as indefinite. The Examiner suggested changing “A hyperthermia method of malignant tumor” to “A hyperthermia method for treating a malignant tumor.” Claim 20 has been amended as suggested by the Examiner.

Claims 1, 4-6, 8, 9, 11, 12, 14, 15, 17, 18, 19, 20, 23, 24, 26, 27, 29, 30, and 31 have been rejected under 35 U.S.C. § 103(a) as obvious over Jpn J Cancer Research, 1998, 89:463-470 (Yanase et al.) in view of Clinical Cancer Research, 2002, 8:2775-2781 (O'Day et al.). Claims 1, 15, 17, 18, 24, 26, 27, 29, 30, and 31 have been cancelled.

The Examiner states that Yanase et al. teach a hyperthermia agent for treating a malignant tumor comprising magnetite cationic liposomes and that

O'Day et al. teaches the administration of cytokines to treat cancer patients.

The Office Action states that since both references are directed to similar treatment that it would be *prima facie* obvious to combine their treatments to treat tumors.

The Declaration provides information regarding the unexpectedly improved results which are provided by a treatment for a tumor which combines hyperthermia and cytokine. The Declaration explains improved results regarding various measures including complete regression, tumor size, and survival rate. For brevity, only the complete regression will be discussed here.

The unexpected superiority in a property can rebut *prima facie* obviousness. *See In re Chupp*, 2 USPQ2d 1437, 1439 (Fed. Cir. 1987); MPEP § 716.02(a). As demonstrated in the attached Declaration Under 37 C.F.R. § 1.132 ("Declaration"), synergistic and unexpected results have been demonstrated regarding the invention recited in the claims. For example, evidence of the complete regression of a tumor ("CR") was provided in the Declaration. When hyperthermia is utilized by itself as described in the present application or as described in Yanase et al., the CR (for one irradiation) is 0% or 20%, respectively. When treatment by interleukin-2 ("IL-2") by itself is done as described in the present application or as described in O'Day et al. (which includes simultaneous treatment by granulocyte macrophage colony

stimulating factor ("GM-CSF")), the CR is 0% or 15%, respectively. In contrast, the combined treatment of hyperthermia and IL-2 pursuant to the present application provides a CR of 75%, which provides a synergistic and unexpectedly superior result in comparison with the additive results of hyperthermia alone and IL-2 alone.

The treatment with only GM-CSF as described in the present application provides a CR of 0%. The treatment with the combination of hyperthermia and GM-CSF provides a CR of 40%, which also demonstrates synergism and unexpected superiority relative to the additive results of hyperthermia by itself and GM-CSF by itself. Thus, unexpected and substantially improved results have been demonstrated.

When an applicant demonstrates substantially improved results and states that the results were unexpected, this should suffice to establish unexpected results in the absence of evidence to the contrary. *See In re Soni*, 34 USPQ2d 1684, 1688 (Fed. Cir. 1995). Thus, the unexpected results of the claimed invention demonstrate unobviousness. Accordingly, Applicants respectfully request that the patentability of the claims of the present application be acknowledged.

Applicants respectfully request a two month extension of time for responding to the Office Action. **The fee of \$450.00 for the extension is**

provided for in the charge authorization presented in the PTO Form 2038, Credit Card Payment form, provided herewith.

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In light of the foregoing, the application is now believed to be in proper form for allowance of all claims and notice to that effect is earnestly solicited.

Respectfully submitted,
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enc: Declaration Under 37 CFR 1.132
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